

| Ref # | Hits | Search Query | DBs | Default Operator | Plurals | Time Stamp |
|-------|------|--|--|------------------|---------|------------------|
| L1 | 1 | NMR and "N15-Bcl-XL" | US-PGPUB; USPAT; EPO; DERWENT | OR | ON | 2005/08/16 09:46 |
| L2 | 1 | "N15-Bcl-XL" | US-PGPUB; USPAT; EPO; DERWENT | OR | ON | 2005/08/16 09:46 |
| L3 | 85 | "TCTP" | US-PGPUB; USPAT; EPO; DERWENT | OR | ON | 2005/08/16 09:46 |
| L4 | 7 | "TCTP" and Bcl-2 | US-PGPUB; USPAT; EPO; DERWENT | OR | ON | 2005/08/16 09:46 |
| L5 | 7 | "TCTP" and Bcl-2 | US-PGPUB; USPAT; EPO; DERWENT | OR | ON | 2005/08/16 09:46 |
| L6 | 1 | "TCTP" and Bcl-2 and "13C labeling" | US-PGPUB; USPAT; EPO; DERWENT | OR | ON | 2005/08/16 09:46 |
| L7 | 7 | "TCTP" and Bcl-2 and protein | US-PGPUB; USPAT; EPO; DERWENT | OR | ON | 2005/08/16 09:46 |
| L8 | 159 | Bcl-XL and Bcl-2 and NMR | US-PGPUB; USPAT; EPO; DERWENT | OR | ON | 2005/08/16 10:06 |
| L9 | 740 | "Bcl-XL" or "Bcl-2" same NMR | US-PGPUB; USPAT; EPO; DERWENT | OR | ON | 2005/08/16 09:47 |
| L10 | 740 | "Bcl-XL" or "Bcl-2" same NMR | US-PGPUB; USPAT; EPO; DERWENT | OR | ON | 2005/08/16 09:47 |
| L11 | 45 | bcl-2 and BH3 same antibody | US-PGPUB; USPAT; EPO; DERWENT | OR | ON | 2005/08/16 09:47 |
| L12 | 16 | Bcl-XL and Bcl-2 and NMR and 530/350.ccls. | US-PGPUB; USPAT; EPO; DERWENT | OR | ON | 2005/08/16 09:48 |

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| L13 | 2 | Bcl-XL and Bcl-2 and NMR and 530/327.ccls. | US-PGPUB; USPAT; EPO; DERWENT | OR | ON | 2005/08/16 09:48 |
| L14 | 2 | Bcl-XL and Bcl-2 and NMR and 530/326.ccls. | US-PGPUB; USPAT; EPO; DERWENT | OR | ON | 2005/08/16 09:48 |
| L15 | 1 | Bcl-XL and Bcl-2 and NMR and 514/617.ccls. | US-PGPUB; USPAT; EPO; DERWENT | OR | ON | 2005/08/16 09:48 |
| L16 | 9 | Bcl-XL and Bcl-2 and NMR and 514/12.ccls. | US-PGPUB; USPAT; EPO; DERWENT | OR | ON | 2005/08/16 09:48 |
| L17 | 10 | Bcl-XL and Bcl-2 and NMR and 435/7.1.ccls. | US-PGPUB; USPAT; EPO; DERWENT | OR | ON | 2005/08/16 09:48 |
| L18 | 3 | Bcl-XL and Bcl-2 and NMR and 530/388.8.ccls. | US-PGPUB; USPAT; EPO; DERWENT | OR | ON | 2005/08/16 10:06 |
| S1 | 1 | NMR and "N15-Bcl-XL" | US-PGPUB; USPAT; EPO; DERWENT | OR | ON | 2004/11/05 15:20 |
| S2 | 1 | "N15-Bcl-XL" | US-PGPUB; USPAT; EPO; DERWENT | OR | ON | 2004/11/05 15:30 |
| S3 | 76 | "TCTP" | US-PGPUB; USPAT; EPO; DERWENT | OR | ON | 2004/11/05 15:31 |
| S4 | 4502 | "TCTP" or TR3 | US-PGPUB; USPAT; EPO; DERWENT | OR | ON | 2004/11/05 15:31 |
| S5 | 7 | "TCTP" and Bcl-2 | US-PGPUB; USPAT; EPO; DERWENT | OR | ON | 2004/11/05 15:31 |
| S6 | 4 | "TCTP" and Bcl-2 and measuring | US-PGPUB; USPAT; EPO; DERWENT | OR | ON | 2004/11/05 16:03 |

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| S7 | 1 | "TCTP" and Bcl-2 and "13C labeling" | US-PGPUB; USPAT; EPO; DERWENT | OR | ON | 2004/11/05 16:03 |
| S8 | 1 | "TCTP" and Bcl-2 and "13C" | US-PGPUB; USPAT; EPO; DERWENT | OR | ON | 2004/11/05 16:03 |
| S9 | 7 | "TCTP" and Bcl-2 and protein | US-PGPUB; USPAT; EPO; DERWENT | OR | ON | 2004/11/08 12:01 |
| S10 | 117 | Bcl-XL and Bcl-2 and NMR | US-PGPUB; USPAT; EPO; DERWENT | OR | ON | 2005/08/16 09:47 |
| S11 | 117 | "Bcl-XL" and "Bcl-2" and NMR | US-PGPUB; USPAT; EPO; DERWENT | OR | ON | 2004/11/08 12:01 |
| S12 | 11 | "Bcl-XL" and "Bcl-2" same NMR | US-PGPUB; USPAT; EPO; DERWENT | OR | ON | 2004/11/08 13:12 |
| S13 | 581 | "Bcl-XL" or "Bcl-2" same NMR | US-PGPUB; USPAT; EPO; DERWENT | OR | ON | 2004/11/08 13:13 |
| S14 | 25 | "Bcl-2" same NMR | US-PGPUB; USPAT; EPO; DERWENT | OR | ON | 2004/11/09 10:29 |
| S15 | 37 | bcl-2 and BH3 same antibody | US-PGPUB; USPAT; EPO; DERWENT | OR | ON | 2004/11/09 10:30 |
| S16 | 5 | "190965".pn. | US-PGPUB; USPAT; EPO; DERWENT | OR | ON | 2004/11/10 10:56 |

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L1 QUE BCL-XL AND BCL-2 AND NMR

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|-----|-----|-------------|
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L3 ANSWER 1 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN
TI Methods and compounds useful to induce apoptosis in cancer cells

L3 ANSWER 2 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 1
TI An inhibitor of Bcl-2 family proteins induces
regression of solid tumours

L3 ANSWER 3 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN
TI Conversion of apoptotic proteins

L3 ANSWER 4 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN
TI Solution structure of Bcl-w determined by NMR spectrometry and its use for screening and design of interacting compounds

L3 ANSWER 5 OF 31 MEDLINE on STN
TI Characterization of protein-ligand interactions by high-resolution solid-state NMR spectroscopy.

L3 ANSWER 6 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN
TI Solution Conformations of Wild-Type and Mutated Bak BH3 Peptides via Dynamical Conformational Sampling and Implication to Their Binding to Antiapoptotic Bcl-2 Proteins

L3 ANSWER 7 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 2
TI Rational design and real time, in-cell detection of the proapoptotic activity of a novel compound targeting Bcl-XL

L3 ANSWER 8 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 3
TI Small-molecule inhibitors of Bcl-2 protein

L3 ANSWER 9 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 4
TI Structural studies of apoptosis and ion transport regulatory proteins in membranes

L3 ANSWER 10 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 5
TI Defining the p53 DNA-binding domain/Bcl-xL-binding interface using NMR

L3 ANSWER 11 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 6
TI Solution Structure of Human BCL-w: Modulation of Ligand Binding by the C-Terminal Helix

L3 ANSWER 12 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 7
TI Cancer Prevention by Tea Polyphenols Is Linked to Their Direct Inhibition of Antiapoptotic Bcl-2-Family Proteins

L3 ANSWER 13 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 8
TI Discovery, Characterization, and Structure-Activity Relationships Studies of Proapoptotic Polyphenols Targeting B-Cell Lymphocyte/Leukemia-2 Proteins

L3 ANSWER 14 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 9
TI Solution Structure of the BHRF1 Protein From Epstein-Barr Virus, a Homolog of Human Bcl-2

L3 ANSWER 15 OF 31 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
TI Novel chemically-stabilized helices of the BCL-2 family induce apoptosis of leukemia cells.

L3 ANSWER 16 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 10
TI A Novel Approach for Characterizing Protein Ligand Complexes: Molecular Basis for Specificity of Small-Molecule Bcl-2 Inhibitors

L3 ANSWER 17 OF 31 MEDLINE on STN DUPLICATE 11
TI Enhanced resistance to salt, cold and wound stresses by overproduction of animal cell death suppressors Bcl-xL and Ced-9 in tobacco cells - their possible contribution through improved function of organelle.

L3 ANSWER 18 OF 31 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on
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TI A view to a kill: Ligands for Bcl-2 family proteins.

L3 ANSWER 19 OF 31 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on
STN

TI Identification of small molecular inhibitors of BH3 and Bcl-xL interaction.

L3 ANSWER 20 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 12

TI Discovery of Small-Molecule Inhibitors of Bcl-2 through Structure-Based Computer Screening

=> d ti 21-38

L3 ANSWER 21 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 13

TI Solution structure of the antiapoptotic protein bcl-2

L3 ANSWER 22 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 14

TI Identification of small-molecule inhibitors of interaction between the BH3 domain and Bcl-XL

L3 ANSWER 23 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 15

TI NMR Studies of the Anti-Apoptotic Protein Bcl-xL in Micelles

L3 ANSWER 24 OF 31 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on
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TI Privileged molecules for protein binding identified from NMR-based screening.

L3 ANSWER 25 OF 31 MEDLINE on STN DUPLICATE 16

TI Rationale for Bcl-xL/Bad peptide complex formation from structure, mutagenesis, and biophysical studies.

L3 ANSWER 26 OF 31 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on
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TI Targeting the mitochondrial redox state of leukemia and lymphoma cells with PK11195 for effective therapy.

L3 ANSWER 27 OF 31 MEDLINE on STN DUPLICATE 17

TI An approach for high-throughput structure determination of proteins by NMR spectroscopy.

L3 ANSWER 28 OF 31 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on
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TI Assessing pore formation by BCL-2 during apoptosis in cell lines and human leukemic cells: Cysteine 158 in the alpha 5 helical loop is in an aqueous environment.

L3 ANSWER 29 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 18

TI Refolding, Purification, and Characterization of a Loop Deletion Mutant of Human Bcl-2 from Bacterial Inclusion Bodies

L3 ANSWER 30 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 19

TI Recombinant mouse Bcl-2(1-203). Two domains connected by a long protease-sensitive linker

L3 ANSWER 31 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 20

TI X-ray and NMR structure of human Bcl-xL, an inhibitor of programmed cell death

=> d ab bib 2, 7, 8, 10, 18, 23, 31

L3 ANSWER 2 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 1

AB Proteins in the Bcl-2 family are central regulators of programmed cell death, and members that inhibit apoptosis, such as Bcl-XL and Bcl-2, are overexpressed in many cancers and contribute to tumor initiation, progression and resistance to therapy. Bcl-XL expression correlates with chemo-resistance of tumor cell lines, and redns. in Bcl-2 increase sensitivity to anticancer drugs and enhance in vivo survival. The development of inhibitors of these proteins as potential anticancer therapeutics has been previously explored, but obtaining potent small-mol. inhibitors has proved difficult owing to the necessity of targeting a protein-protein interaction. Here, using NMR-based screening, parallel synthesis and structure-based design, the authors have discovered ABT-737, a small-mol. inhibitor of the antiapoptotic proteins Bcl-2, Bcl-XL and Bcl-w, with an affinity two to three orders of magnitude more potent than previously reported compds. Mechanistic studies reveal that ABT-737 does not directly initiate the apoptotic process, but enhances the effects of death signals, displaying synergistic cytotoxicity with chemotherapeutics and radiation. ABT-737 exhibits single-agent-mechanism-based killing of cells from lymphoma and small-cell lung carcinoma lines, as well as primary patient-derived cells, and in animal models, ABT-737 improves survival, causes regression of established tumors, and produces cures in a high percentage of the mice.

AN 2005:467373 CAPLUS

TI An inhibitor of Bcl-2 family proteins induces regression of solid tumours

AU Oltersdorf, Tilman; Elmore, Steven W.; Shoemaker, Alexander R.; Armstrong, Robert C.; Augeri, David J.; Belli, Barbara A.; Bruncko, Milan; Deckwerth, Thomas L.; Dinges, Jurgen; Hajduk, Philip J.; Joseph, Mary K.; Kitada, Shinichi; Korsmeyer, Stanley J.; Kunzer, Aaron R.; Letai, Anthony; Li, Chi; Mitten, Michael J.; Nettesheim, David G.; Ng, Shi Chung; Nimmer, Paul M.; O'Connor, Jacqueline M.; Oleksijew, Anatol; Petros, Andrew M.; Reed, John C.; Shen, Wang; Tahir, Stephen K.; Thompson, Craig B.; Tomaselli, Kevin J.; Wang, Baole; Wendt, Michael D.; Zhang, Haichao; Fesik, Stephen W.; Rosenberg, Saul H.

CS Idun Pharmaceuticals, San Diego, CA, 92121, USA

SO Nature (London, United Kingdom) (2005), 435(7042), 677-681

CODEN: NATUAS; ISSN: 0028-0836

PB Nature Publishing Group

DT Journal

LA English

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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 2

AB Antiapoptotic Bcl-2-family proteins Bcl-2 and Bcl-XL have been recently validated as drug discovery targets for cancer. Here, by using a combination of mol. modeling, NMR-based structural anal., fluorescence polarization assays, and cell-based assays, we have designed and characterized a novel proapoptotic compound targeting these proteins. Our compound, Apogossypol, is capable of binding and inhibiting Bcl-2 and Bcl-XL with high affinity and induces apoptosis of tumor cell lines. Mechanistic studies on the action of our compound were also performed via confocal microscopy that provided real-time detection of the interaction with Bcl-XL in intact cells. Finally, preliminary data on cells freshly isolated from patients affected by chronic lymphocytic leukemia strongly suggest potential applications of Bcl-2 antagonists as chemosensitizers in cancer therapy.

AN 2004:261470 CAPLUS

DN 141:133679

TI Rational design and real time, in-cell detection of the proapoptotic activity of a novel compound targeting Bcl-XL
AU Becattini, Barbara; Kitada, Shinichi; Leone, Marilisa; Monosov, Edward; Chandler, Sharon; Zhai, Dayong; Kipps, Thomas J.; Reed, John C.; Pellecchia, Maurizio
CS The Burnham Institute, La Jolla, CA, 92037, USA
SO Chemistry & Biology (2004), 11(3), 389-395
CODEN: CBOLE2; ISSN: 1074-5521
PB Cell Press
DT Journal
LA English
RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 3
AB A review. Approaches to drug discovery are varied and range from high-resolution NMR solution structure of targeted mols. to rational design. This review is focused on the use of small-mol. inhibitors of Bcl-2 as therapeutic agents. Members of the Bcl-2 family of proteins are crucial regulators of apoptotic cell death. Human cancers have been found to over-express Bcl-2 and Bcl-XL. Cells with high levels of these antiapoptotic mols. are usually resistant to a wide spectrum of chemotherapeutic drugs. Targeting the Bcl-2 family of proteins with small-mol. inhibitors has therefore become an attractive potential therapy for a variety of cancers. The role of Bcl-2 in sabotaging the success of cytotoxic agents suggests that novel treatments should be devised to target Bcl-2-over-expressing tumor cells and induce apoptosis directly. In this article, we will provide a review of potential small-mol. inhibitors as anticancer agents. The de-regulated over-expression of Bcl-2 and Bcl-XL is directly related to cancer cell survival and resistance to chemotherapeutic drugs, making antagonists or inhibitors of these proteins very promising candidates for use in cancer therapy.

AN 2004:545110 CAPLUS
DN 142:16057
TI Small-molecule inhibitors of Bcl-2 protein
AU Pulley, Heather; Mohammad, Ramzi
CS Division of Hematology and Oncology, Department of Internal Medicine/Karmanos Cancer Institute, Wayne State University School of Medicine, Detroit, MI, 48201, USA
SO Drugs of the Future (2004), 29(4), 369-381
CODEN: DRFUD4; ISSN: 0377-8282
PB Prous Science
DT Journal; General Review
LA English

L3 ANSWER 10 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 5
AB P53 exerts its tumor suppressor activity through both transcription-dependent and transcription-independent processes. Although the transcription-dependent activity of p53 has been extensively studied, the mechanism for transcription-independent p53-mediated tumor suppression is less well known. Recently, it was reported that p53 can directly induce mitochondrial permeabilization and promote apoptosis. This occurs through complexation of the DNA-binding region of p53 with the anti-apoptotic proteins Bcl-xL and Bcl-2 (Mihara, M. et al. (2003) Mol. Cell 11, 577-590). Using NMR spectroscopy we show that the interaction surface on p53 involves the same region that is used by the protein to contact DNA. The p53-binding site on Bcl-xL consists of the carboxy-terminus of the first α -helix, the loop between α 3 and α 4, and the loop between α 5 and α 6 of Bcl-xL. Furthermore, the interaction of p53 with Bcl-xL is blocked by the

binding of a 25-residue peptide derived from the BH3 region of the pro-apoptotic protein referred to as Bad.

AN 2004:114202 CAPLUS
DN 140:266453
TI Defining the p53 DNA-binding domain/Bcl-xL-binding interface using NMR
AU Petros, Andrew M.; Gunasekera, Angelo; Xu, Nan; Olejniczak, Edward T.; Fesik, Stephen W.
CS Global Pharmaceutical Research and Development, Abbott Laboratories, Abbott Park, IL, 60064, USA
SO FEBS Letters (2004), 559(1-3), 171-174
CODEN: FEBLAL; ISSN: 0014-5793
PB Elsevier Science B.V.
DT Journal
LA English
RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 18 OF 31 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2002:500148 BIOSIS
DN PREV200200500148
TI A view to a kill: Ligands for Bcl-2 family proteins.
AU Rutledge, Stacey E. [Reprint author]; Chin, Jason W.; Schepartz, Alanna [Reprint author]
CS Department of Chemistry, Yale University, PO Box 208107, New Haven, CT, 06520-8107, USA
SO Current Opinion in Chemical Biology, (August, 2002) Vol. 6, No. 4, pp. 479-485. print.
ISSN: 1367-5931.
DT Article
General Review; (Literature Review)
LA English
ED Entered STN: 25 Sep 2002
Last Updated on STN: 25 Sep 2002

L3 ANSWER 23 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 15
AB The Bcl-2 family of proteins play a pivotal role in the regulation of programmed cell death. One of the postulated mechanisms for the function of these proteins involves the formation of ion channels in membranes. As a first step to structurally characterize these proteins in a membrane environment, we investigated the structure of a Bcl-xL mutant protein when incorporated into small detergent micelles. This form of Bcl-xL lacks the loop (residues 49-88) between helix 1 and helix 2 and the putative C-terminal transmembrane helix (residues 214-237). Below the critical micelle concentration (CMC), Bcl-xL binds detergents in the hydrophobic groove that binds to pro-apoptotic proteins. However, above the CMC, Bcl-xL undergoes a dramatic conformational change. Using NMR methods, we characterized the secondary structure of Bcl-xL in the micelle-bound form. Like Bcl-xL in aqueous solution, the structure of the protein when dissolved in dodecylphosphocholine (DPC) micelles consists of several α -helices separated by loops. However, the length and position of the individual helices of Bcl-xL in micelles differ from those in aqueous solution. The location of Bcl-xL within the micelle was examined from the anal. of protein-detergent NOEs and limited proteolysis. In addition, the mobility of the micelle-bound form of Bcl-xL was investigated from NMR relaxation measurements. On the basis of these studies, a model is proposed for the structure, dynamics, and location of Bcl-xL in micelles. In this model, Bcl-xL has a loosely packed, dynamic structure in micelles, with helices 1 and 6 and possibly helix 5 partially buried in

the hydrophobic interior of the micelle. Other parts of the protein are located near the surface or on the outside of the micelle.

AN 2000:567804 CAPLUS
DN 133:292518
TI NMR Studies of the Anti-Apoptotic Protein Bcl-xL in Micelles
AU Losonczi, Judit A.; Olejniczak, Edward T.; Betz, Stephen F.; Harlan, John E.; Mack, Jamey; Fesik, Stephen W.
CS Pharmaceutical Discovery Division, Abbott Laboratories, Abbott Park, IL, 60064, USA
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AB The Bcl-2 family of proteins regulate programmed cell death by an unknown mechanism. Here we describe the crystal and solution structures of a Bcl-2 family member, Bcl-xL. The structures consist of two central, primarily hydrophobic α -helices, which are surrounded by amphipathic helices. A 60-residue loop connecting helices $\alpha 1$ and $\alpha 2$ was found to be flexible and non-essential for anti-apoptotic activity. The three functionally important Bcl-2 homol. regions (BH1, BH2 and BH3) are in close spatial proximity and form an elongated hydrophobic cleft that may represent the binding site for other Bcl-2 family members. The arrangement of the α -helices in Bcl-xL is reminiscent of the membrane translocation domain of bacterial toxins, in particular diphtheria toxin and the colicins. The structural similarity may provide a clue to the mechanism of action of the Bcl-2 family of proteins.
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